Ινστιτούτα

ΙΝΣΤΙΤΟΥΤΟ
ΕΠΙΣΤΗΜΗΣ ΥΛΙΚΩΝ
ΚΑΙ ΥΠΟΛΟΓΙΣΜΩΝ

UNIVERSITY
OF IOANNINA

APPLIED BIOINORGANIC CHEMISTRY GROUP (ABC GROUP)

Professor Sotiris K Hadjikakou
http://users.uoi.gr/shadjika/Hadjikakou_1/Hadjikakou_01.htm

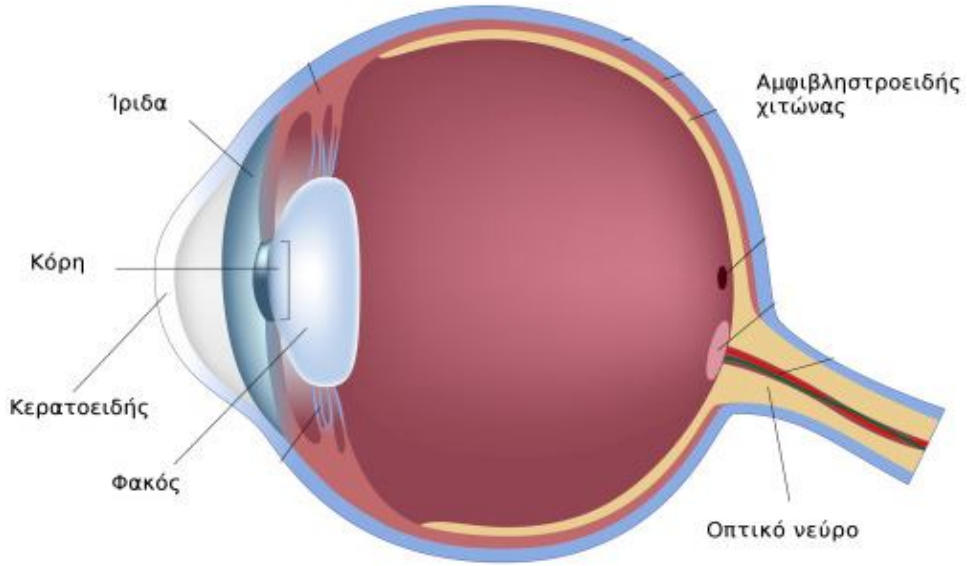
Synthesis and nanodelivery strategies for new targeted therapeutic tools against tumours

Anti-microbial coating innovations to prevent infectious diseases

Study of the mechanism of action of anti-thyroid drugs.

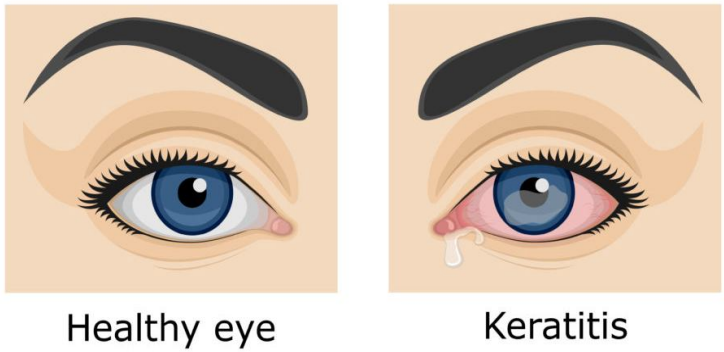
Corneal diseases

- **MK is corneal infection and**
- **Microbial keratitis (MK) is one of the reasons of blindness worldwide**
- **MK can also cause corneal perforations, within less than 24 h**



- **MK is caused from a wide range of bacteria such as**

Pseudomonas aeruginosa (PAO1),
Staphylococcus epidermidis (S. epidermidis)
Staphylococcus aureus (S. aureus)

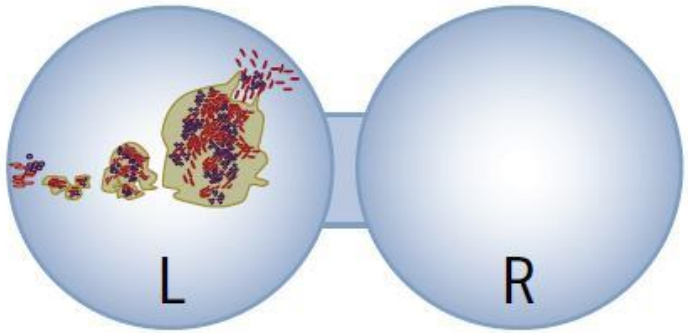


Healthy eye Keratitis

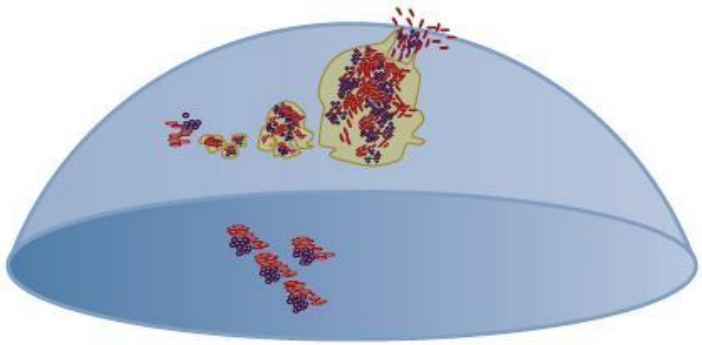
Main symptoms: red eyes, profuse tearing, photophobia, corneal clouding, intense pain

•Contact lenses are risk factors for developing ocular complications such as MK

Although, the incidence of MK is rather low, as compared to other health conditions, however, due to the high number of contact lens wearers (45 million in the United States), there are thousands of cases of MK each year

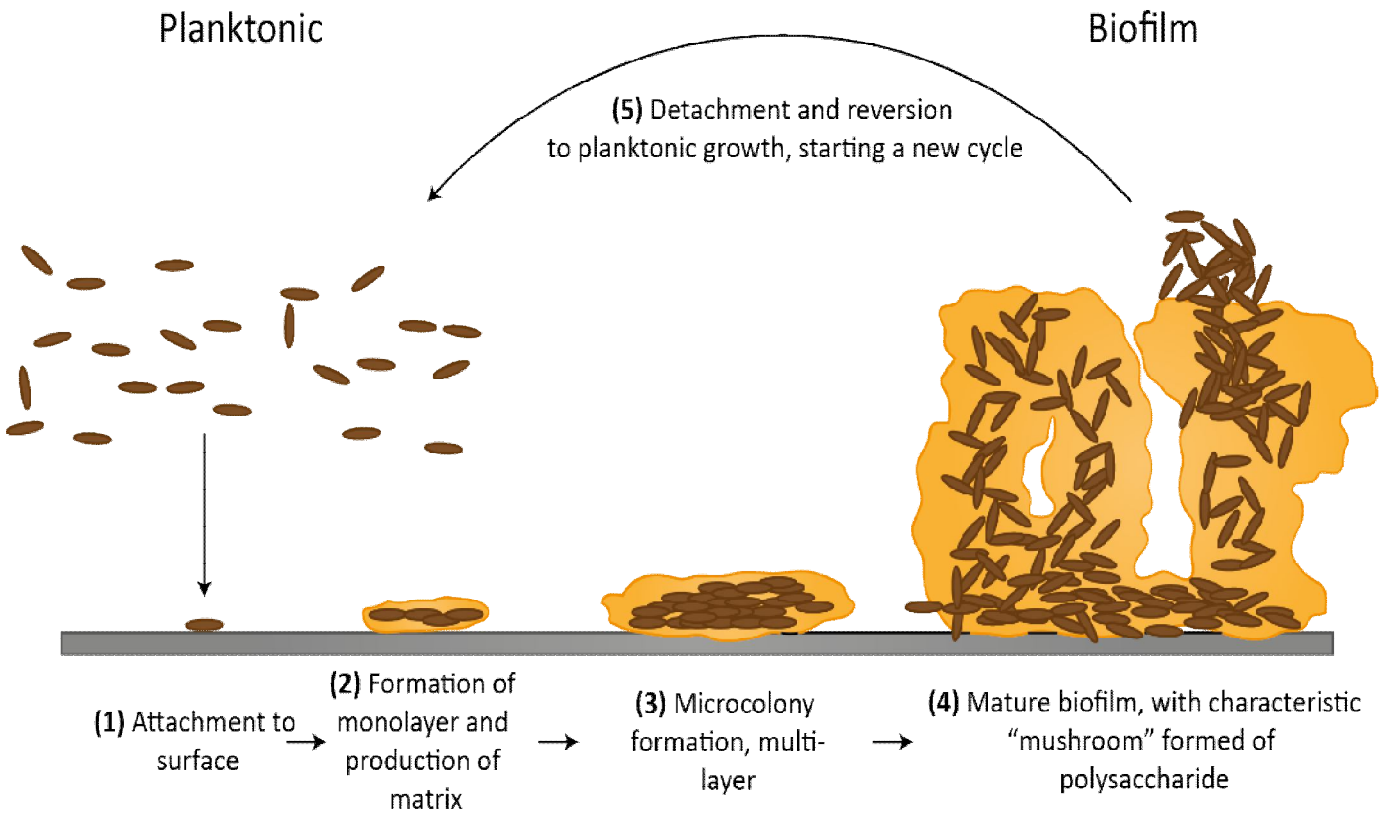


Contaminated contact lens case



Contaminated contact lens

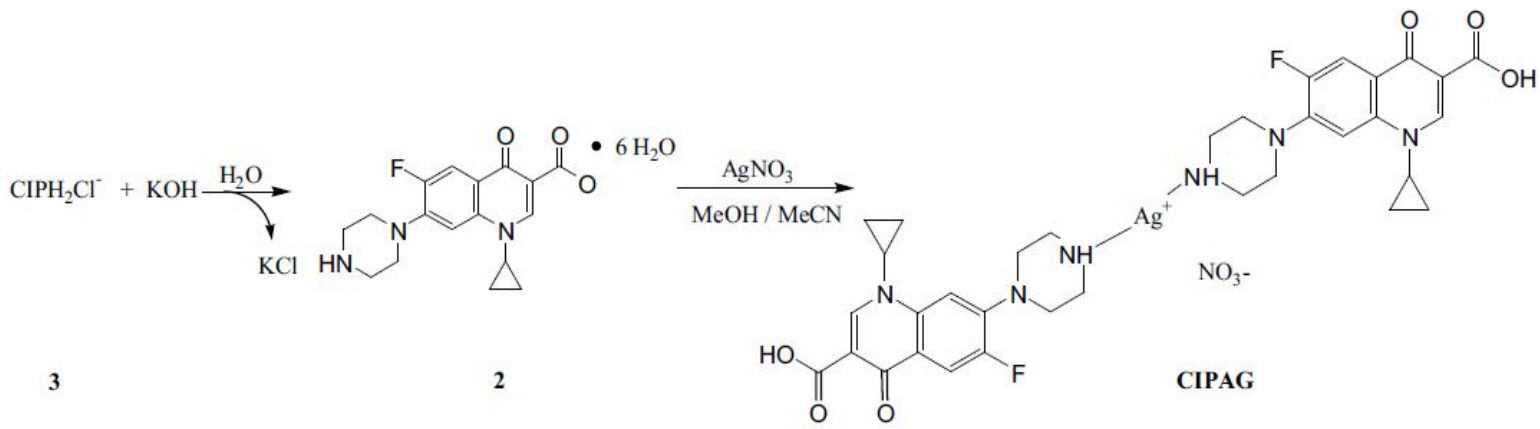
Bacteria can adhere and colonize to lens materials due to their ability to grow as a resistant biofilm on lenses



biofilms represent a major threat during infections

the use of contact lens, which are made by long term or permanent, antimicrobial materials is a research, technological and financial issue of great importance

Conjugate of ciprofloxacin with the silver nitrate $\{[Ag(CIPH)_2]NO_3 \cdot 0.75MeOH \cdot 1.2H_2O\}$ (CIPAG)



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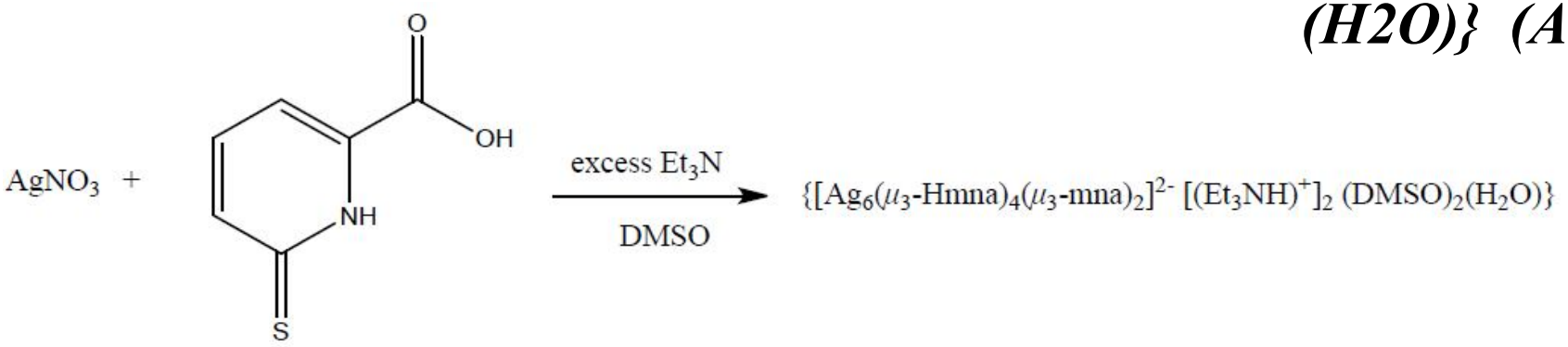
the Metal Organic Framework (MOF) of formula $\{[Ag_6(\mu_3\text{-}HMNA)_4(\mu_3\text{-}MNA)_2]2- \cdot [(Et_3NH)+]2 \cdot (DMSO)_2 \cdot (H2O)\}$ (AGMNA)



H2mna

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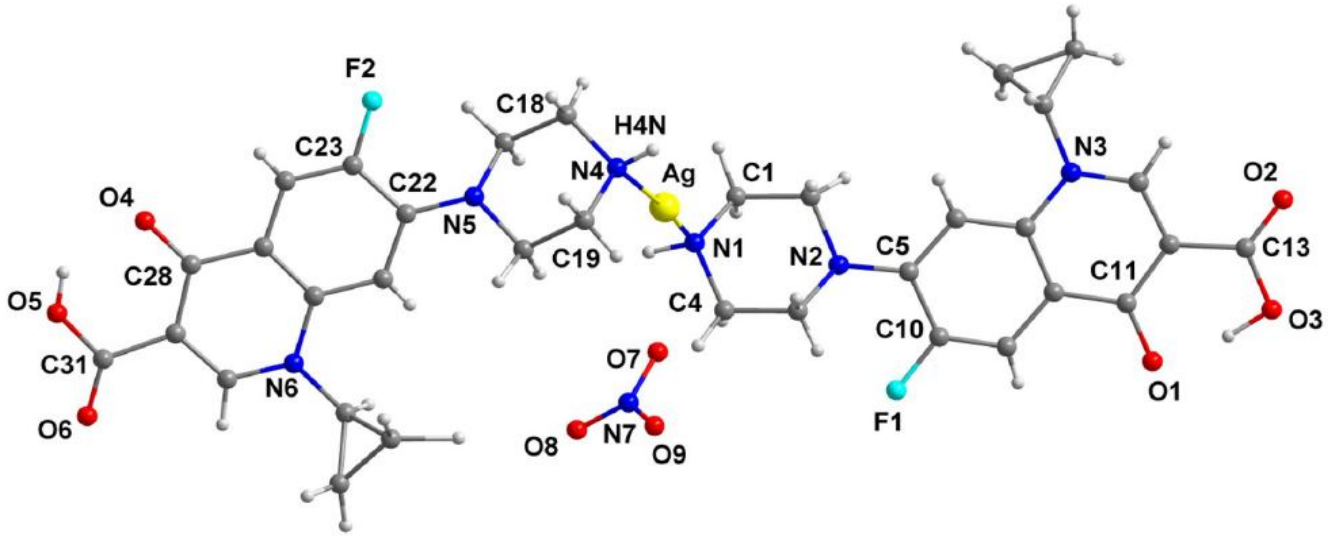
X-Ray studies



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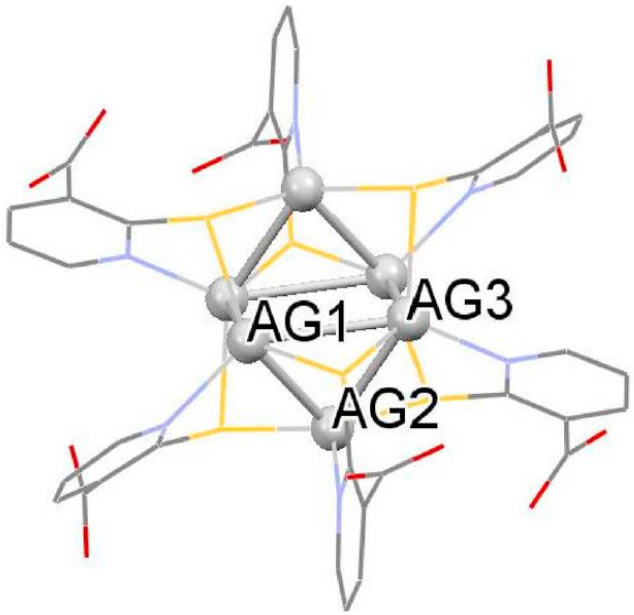

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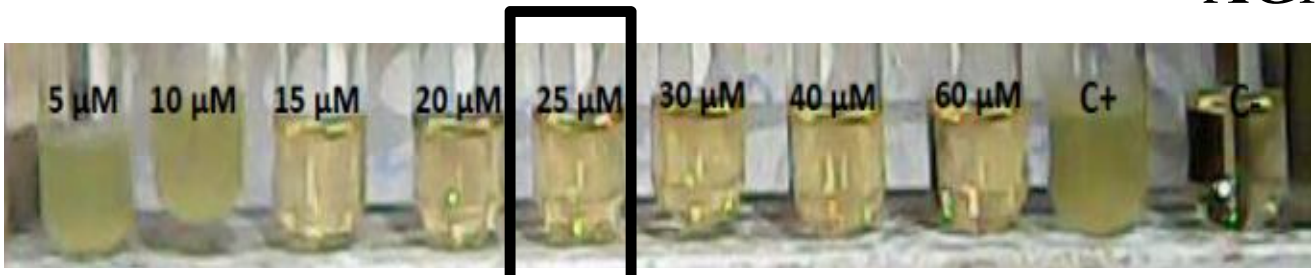
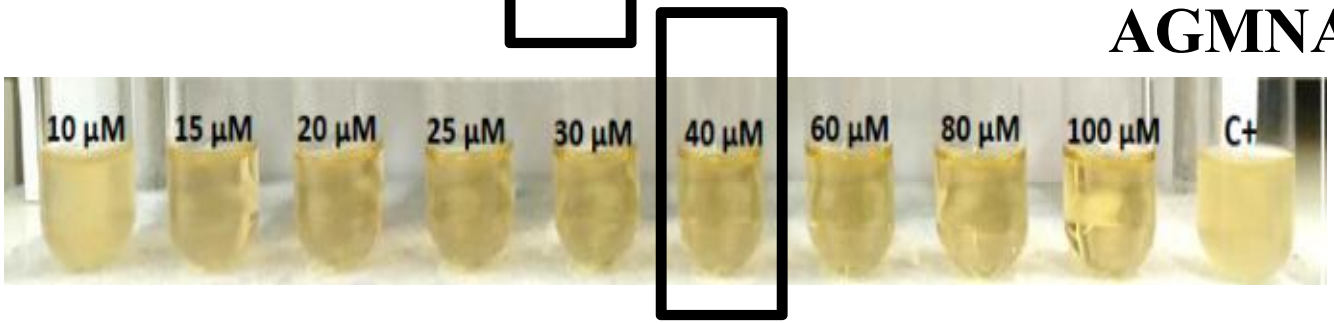
Effects of complex on the growth of microbial strains

Minimal Inhibitory Concentration

AGMNA against *PAO1*



AGMNA against *S. aureus*



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Compound	MIC (μM)		
	PAO1	*S. epidermidis*	*S. aureus*
CIPAG	0.61±0.14	0.46±0.08	0.54±0.07
CIPHCl	1.17±0.22	1.01±0.12	1.45±0.12
AGMNA	25.7±2.4		42.0±0.3
H_2MNA	>300		>300
$AgNO_3$	60	39.4	79.5

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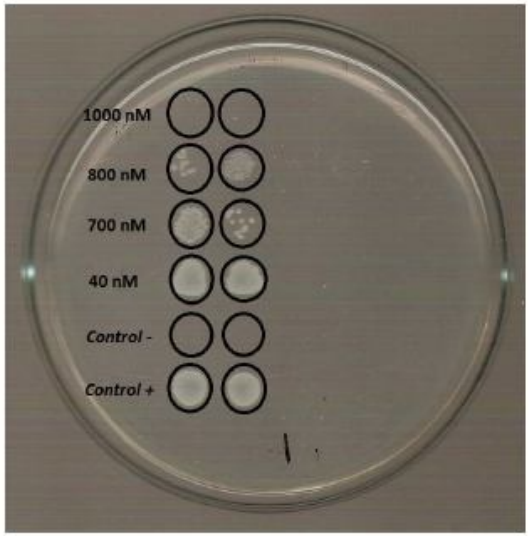
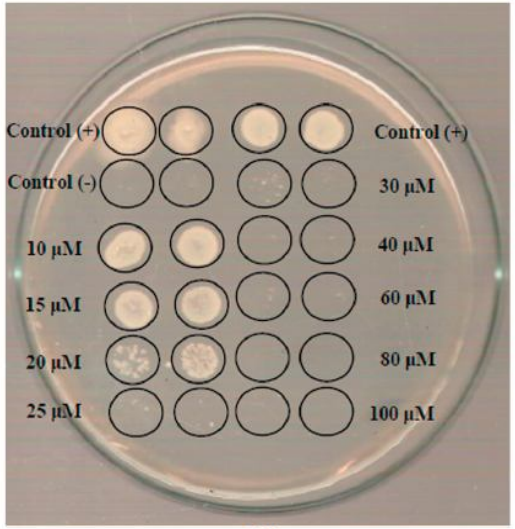
Minimum bactericidal concentration (MBC)

MBC value of CIPAG against *S. aureus*



MBC value of AGMNA against *S. aureus*



(C)

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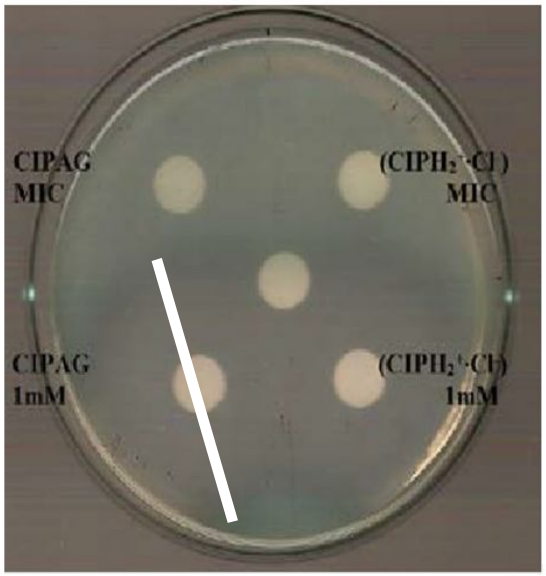
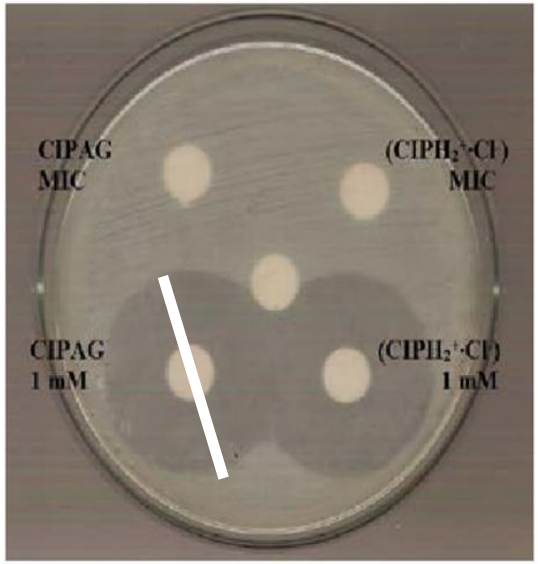
When the value of the MBC/MIC for a compound is ≤ 2, then it is classified into bactericidal one which indicates that it kills 99.9% of the microorganisms. If the MBC/MIC for a compound is ≥ 4 then it is bacteriostatic, it inhibits but not kill the organism

	MBC (μM)		
	PAO1	*S. epidermidis*	*S. aureus*
CIPAG	0.7	0.8	1.0
CIPHCl	1.6	1.6	2.0
AGMNA	61.1		85.7
$AgNO_3$	91.5	140	95
	MBC/MIC		
	PAO1	*S. epidermidis*	*S. aureus*
CIPAG	1.14	1.75	1.86
CIPHCl	1.36	1.48	1.38
AGMNA	2.38		2.04
$AgNO_3$	1.53	3.55	1.19

Inhibition zone

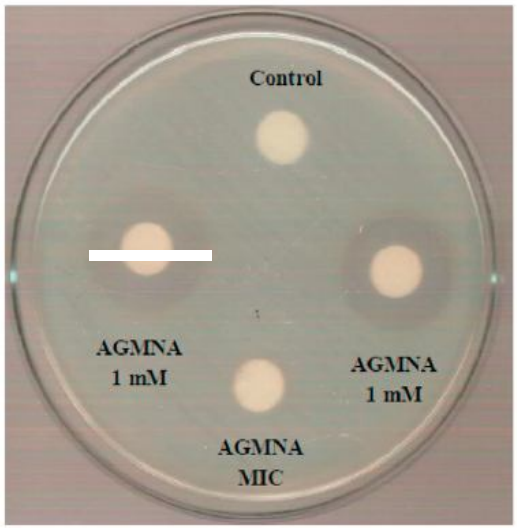


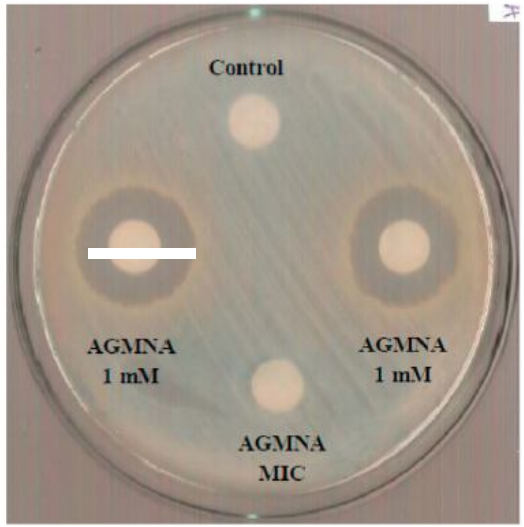


CIPAG

PAO1: **32 mm**

S. aureus: **28 mm**





The eye bulb diameter is 25mm

AGMNA

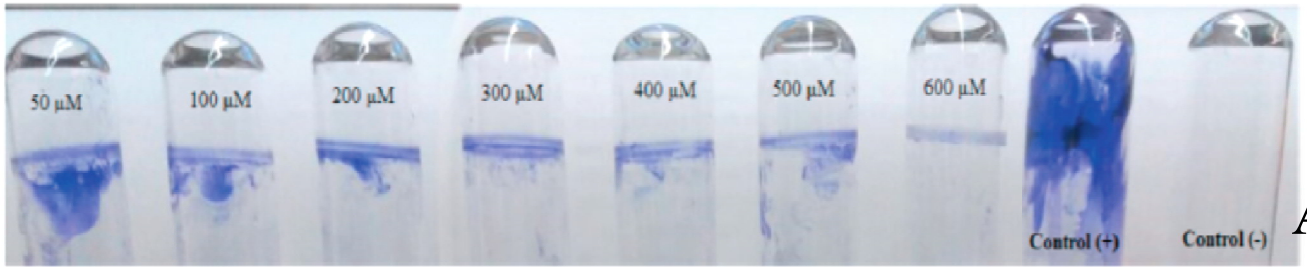
PAO1: **21.8±0.8 mm**

S. aureus: **22.1±0.4 mm**

The biofilm elimination concentration (BEC) of an agent was determined as the concentration required to achieve at least a 99.9% reduction in the viability of biofilm bacteria

CIPAG: 490 µM
CIPH: 897 µM

CIPAG is 1.5 fold more efficient against biofilm than the commercially available antibiotic



AGMNA: 722.6 µM

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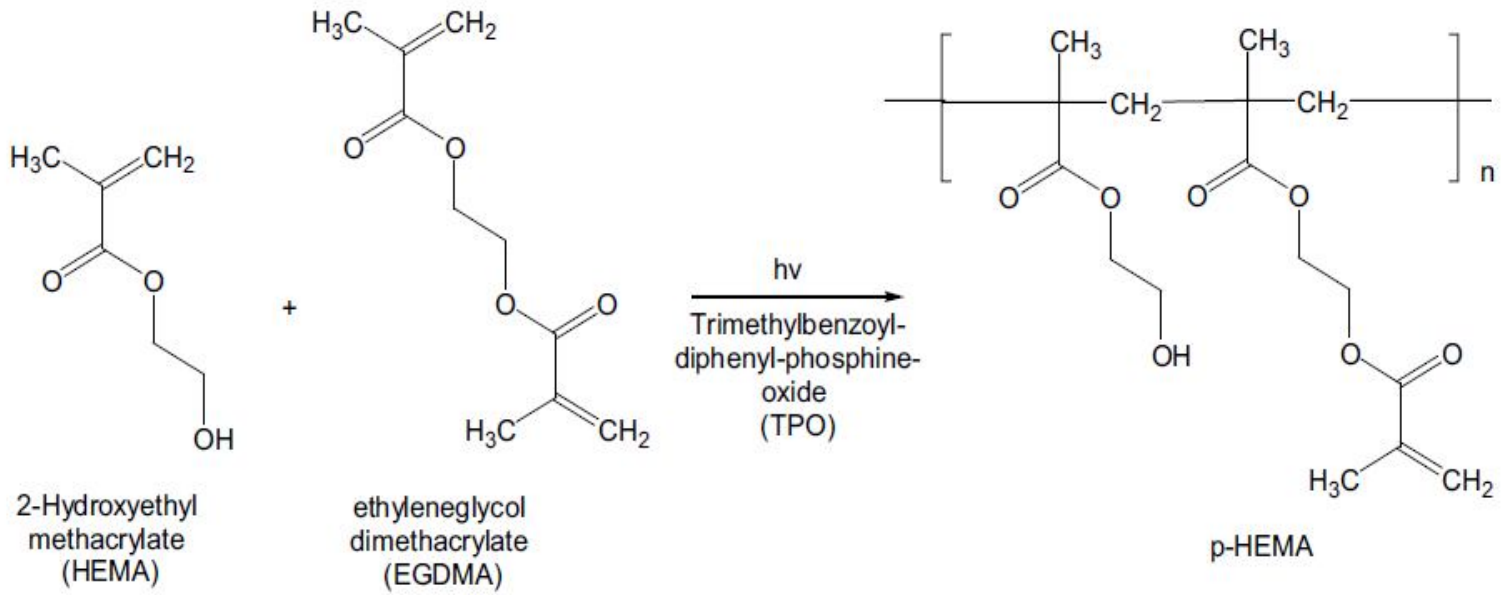
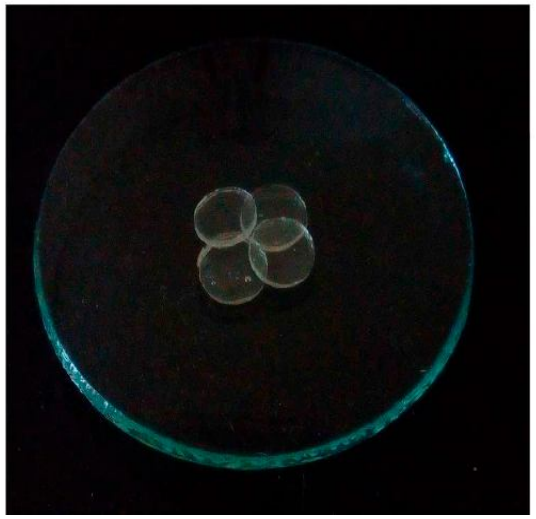
A common type of hydrogel used in contact lenses is poly-HEMA



Hydrogels are soft and rubbery consistence, excellent biocompatibility and high permeability to oxygen, nutrients and other water soluble metabolites making it an excellent material for contact lenses formation

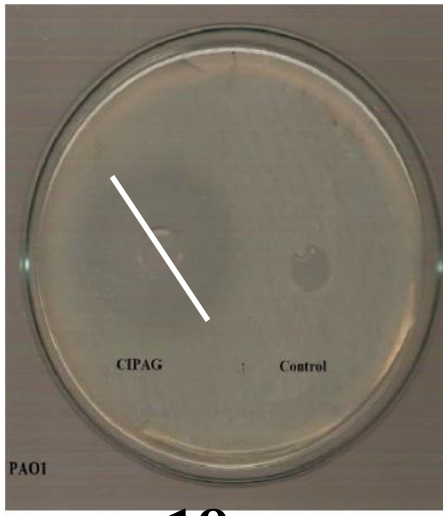




The dispersion of antimicrobials agents into pHEMA was qualitatively verified by:

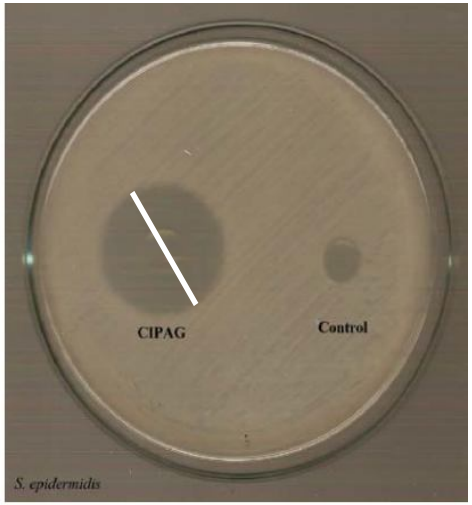
- **Refractive index**
- **Attenuated total reflection spectroscopy (ATR-IR)**
- **Differential Scanning Calorimetry (DSC)**
- **X-ray fluorescence spectroscopy(XRF)**
- **X-ray powder diffraction analysis (XRPD),**
- **Scanning Electron Microscopy (SEM), Energy-dispersive X-ray**
- **spectroscopy (EDX)**

Antibacterial activity of lens

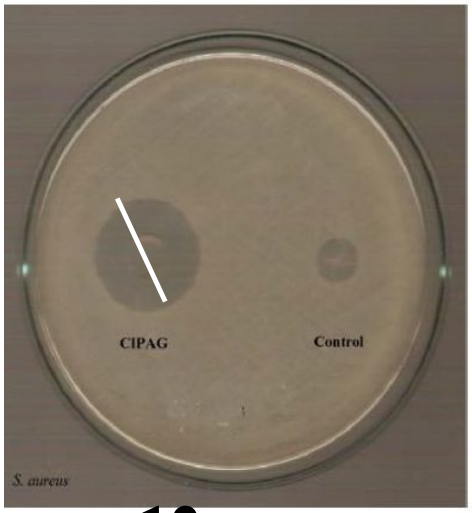
pHEMA@CIPAG



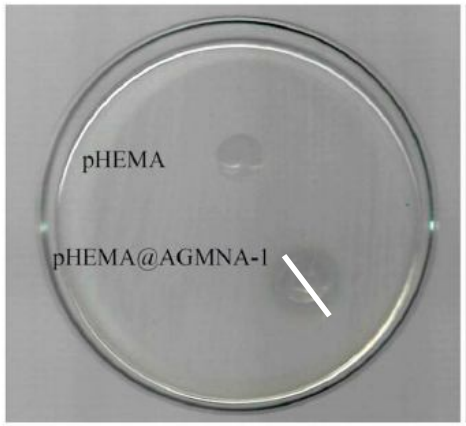
18 mm



16 mm

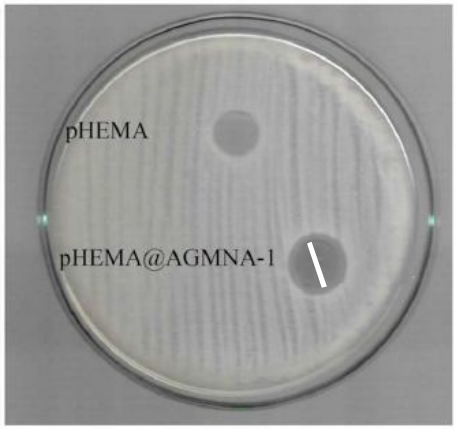


12 mm



14.0 mm

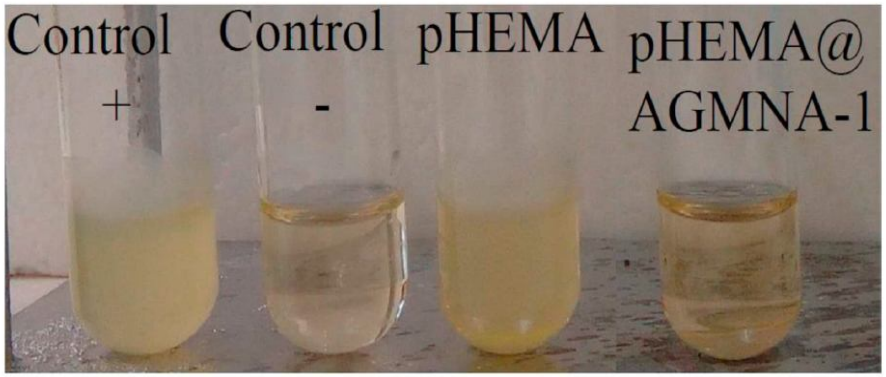
11.3 mm



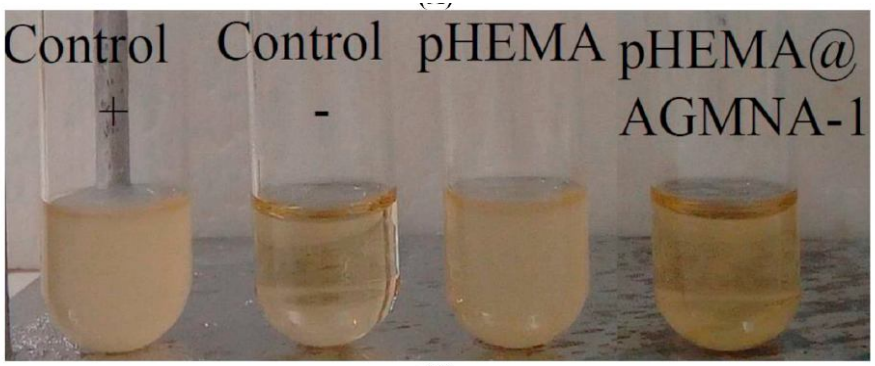
11.8 mm

pHEMA@AGMNA

Microbial viability on lens



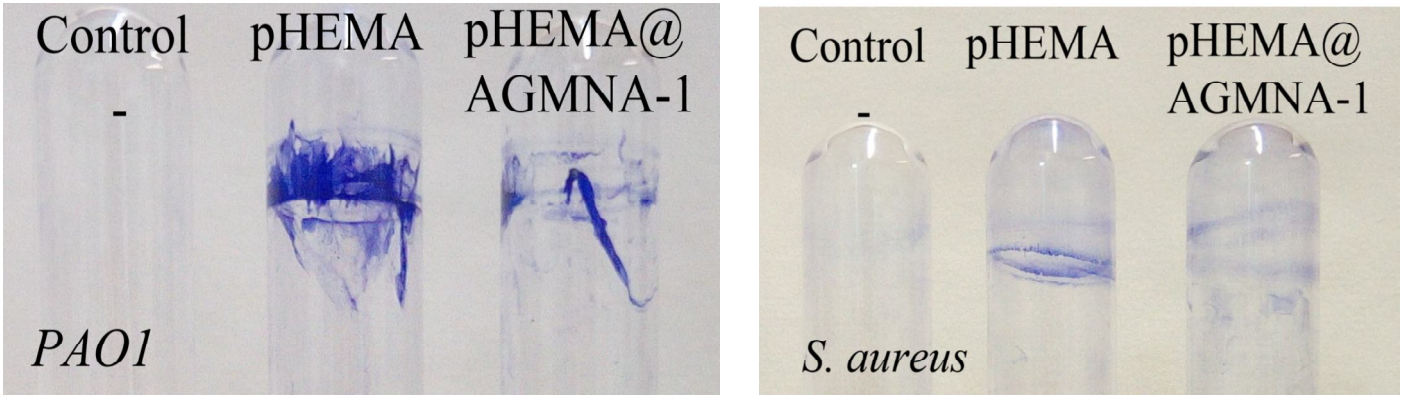
***P. aeruginosa* 0.4 ± 0.1%**



***S. epidermidis* 1.5 ± 0.4%**

***S. aureus* 7.7 ± 0.5%**

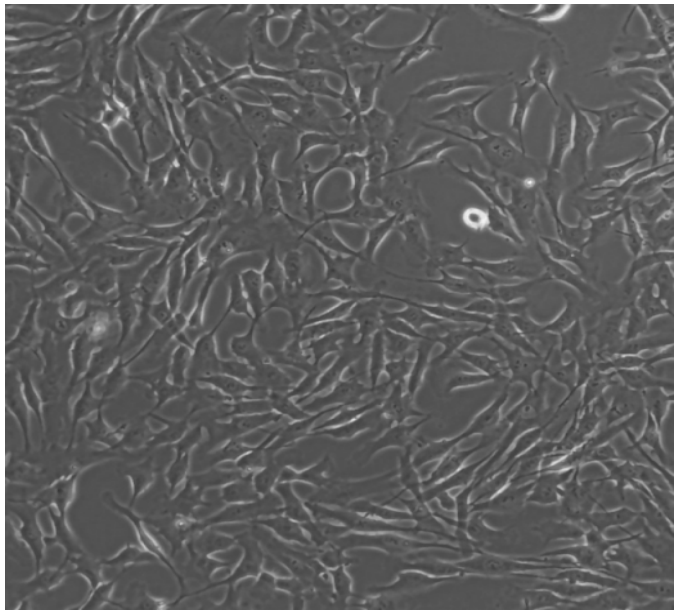
Biofilm elimination pHEMA@ AGMNA



pHEMA@AGMNA lenses eliminate biofilm by 28.7 (P. aeruginosa) and 39.6% (S. aureus)

In vitro toxicity on human corneal epithelial cells (HCEC)

IC_{50} values
CIPAG:15.7 ± 0.4 μM
CIPHCl: 20.5 ± 0.4 μM
H2mna: 20.7 ± 0.4 μM
AGMNA>120 μM.



Cell viability on HCEC

pHEMA@AGMNA-1: 94.3 ± 0.9%

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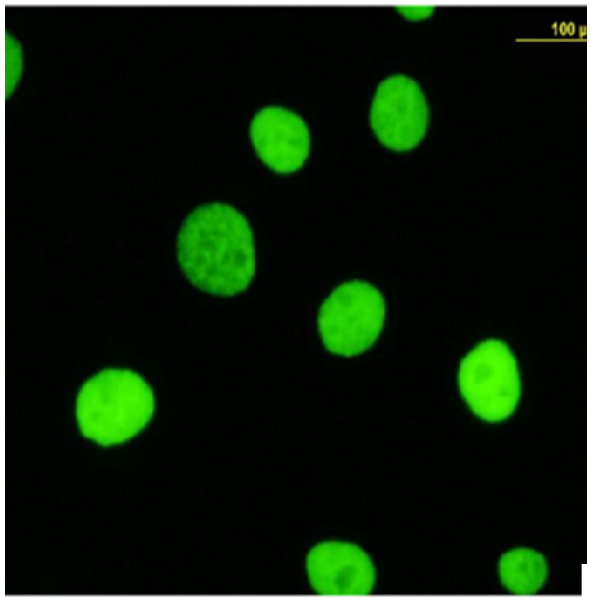
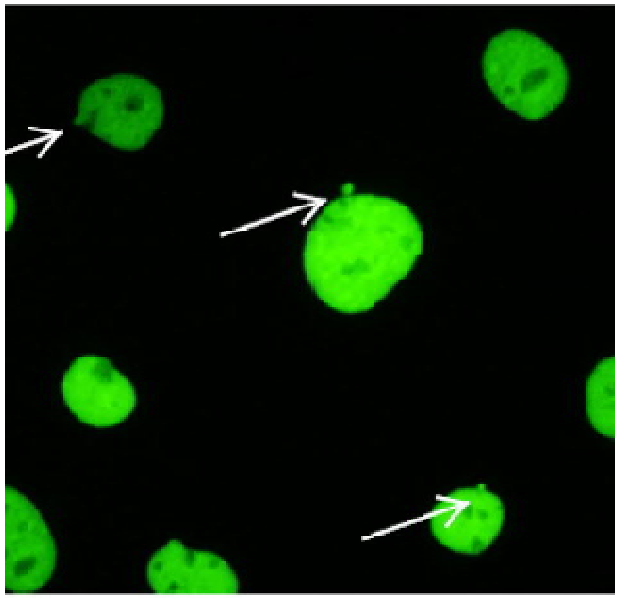
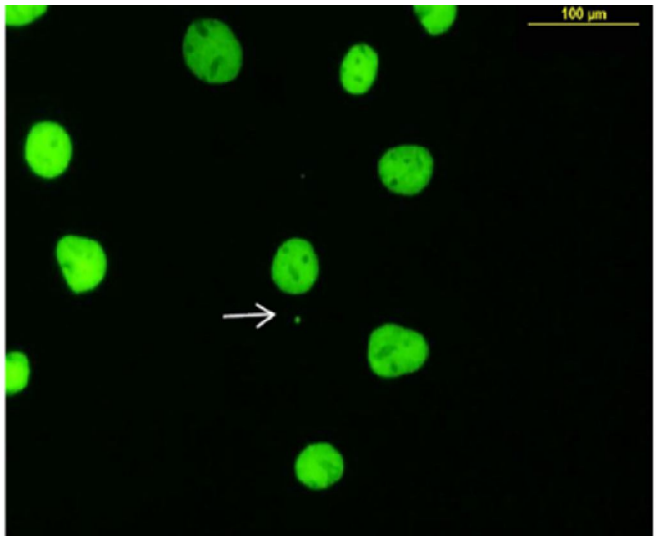


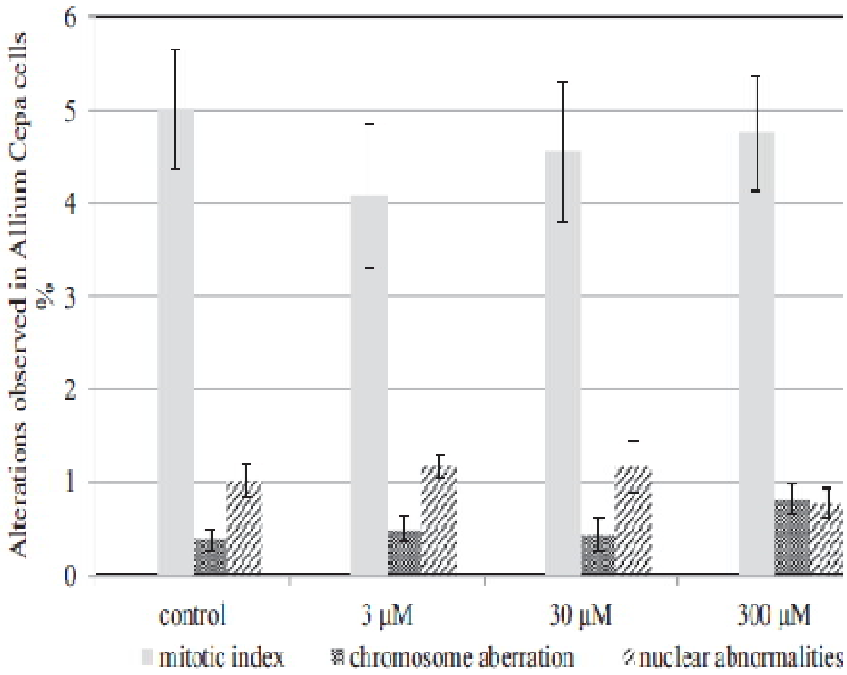


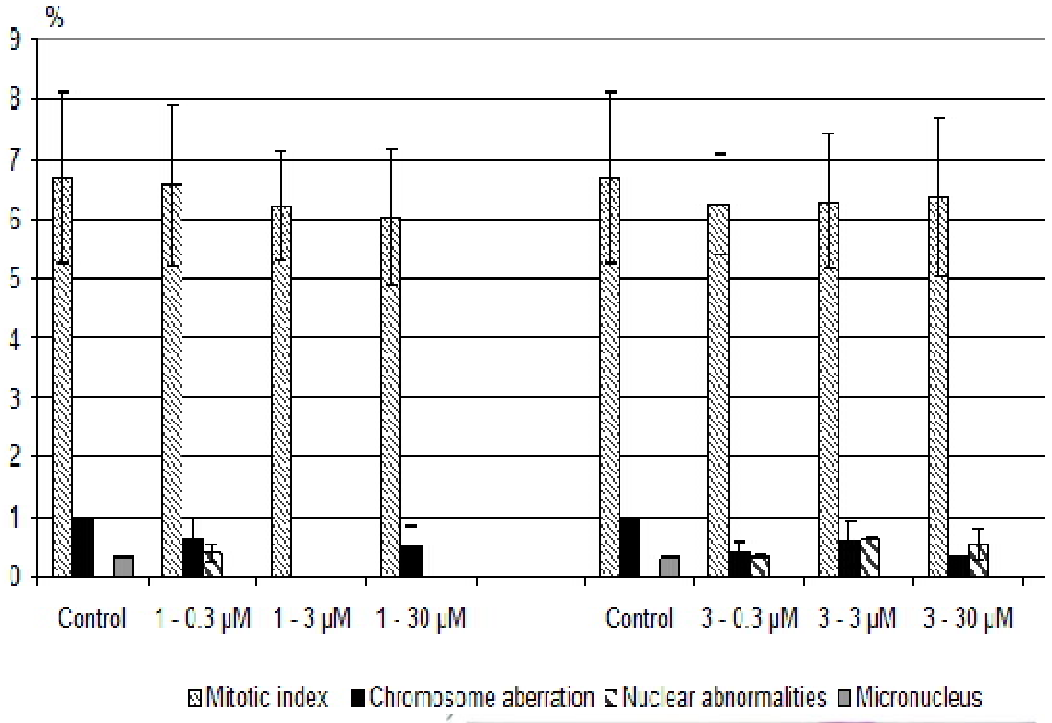


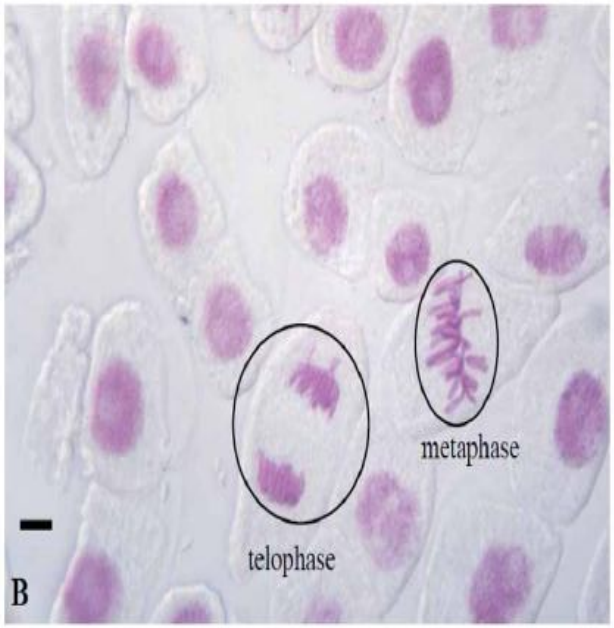
HCEC MN:
3.80 ± 0.19%.
CIPAG:
4.50 ± 0.13%

HCEC MN:
2.20 ± 0.19%.
AGMNA:
2.55 ± 0.13%

Evaluation of genotoxicity by micronucleus assay (MN)

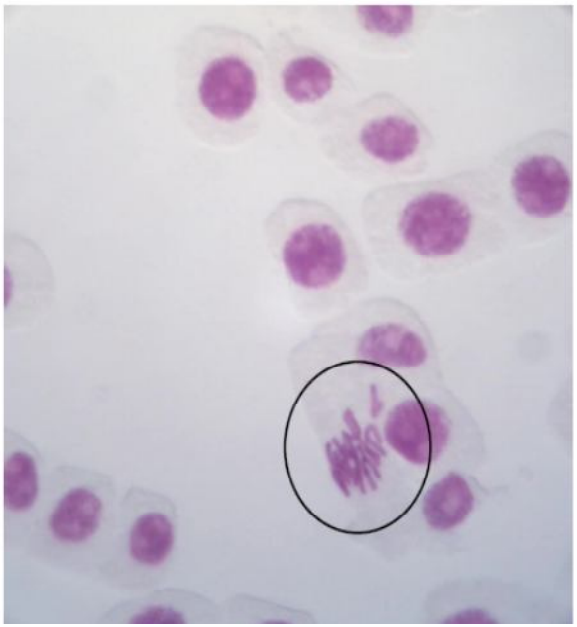






In vivo genotoxicity
Allium cepa assay

Mitotic index
Nuclear Abnormalities

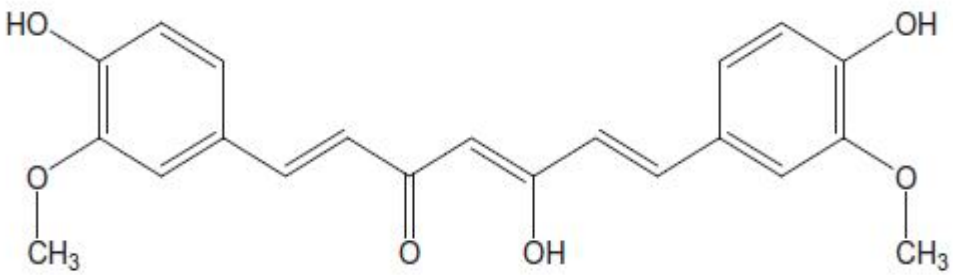


In vivo toxicity
***Artemia salina*, with and without pHEMA@AGMNA.**

No toxicity

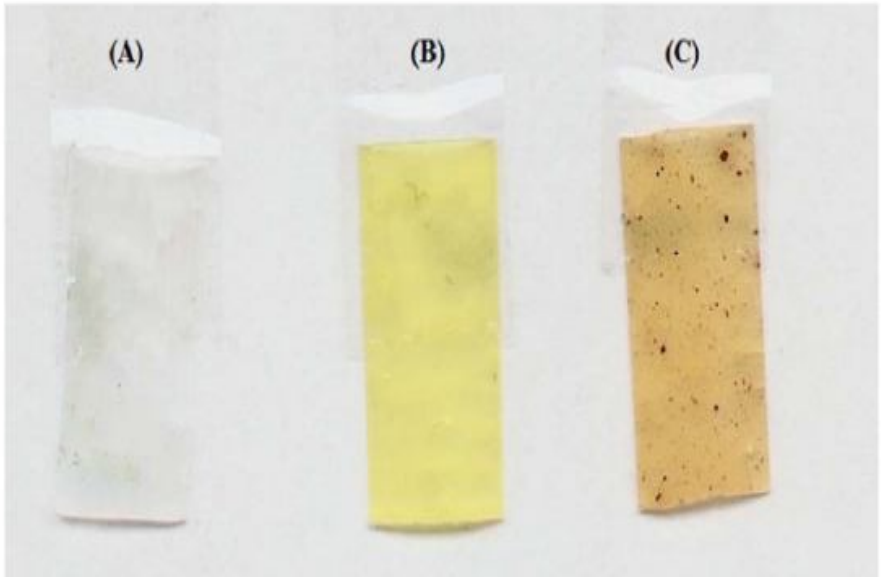
Innovative material containing the natural product

Curcumin has antimicrobial activity



Zinc complexes show excellent antimicrobial activity

Due to the resistance which is developed by microorganisms against antibiotics new metallodrugs are needed



Ribbons of 1 cm width polystyrene (A), polystyrene@curcumin(B) polystyrene@[$ZnI_2(Curc)_2$] (C)

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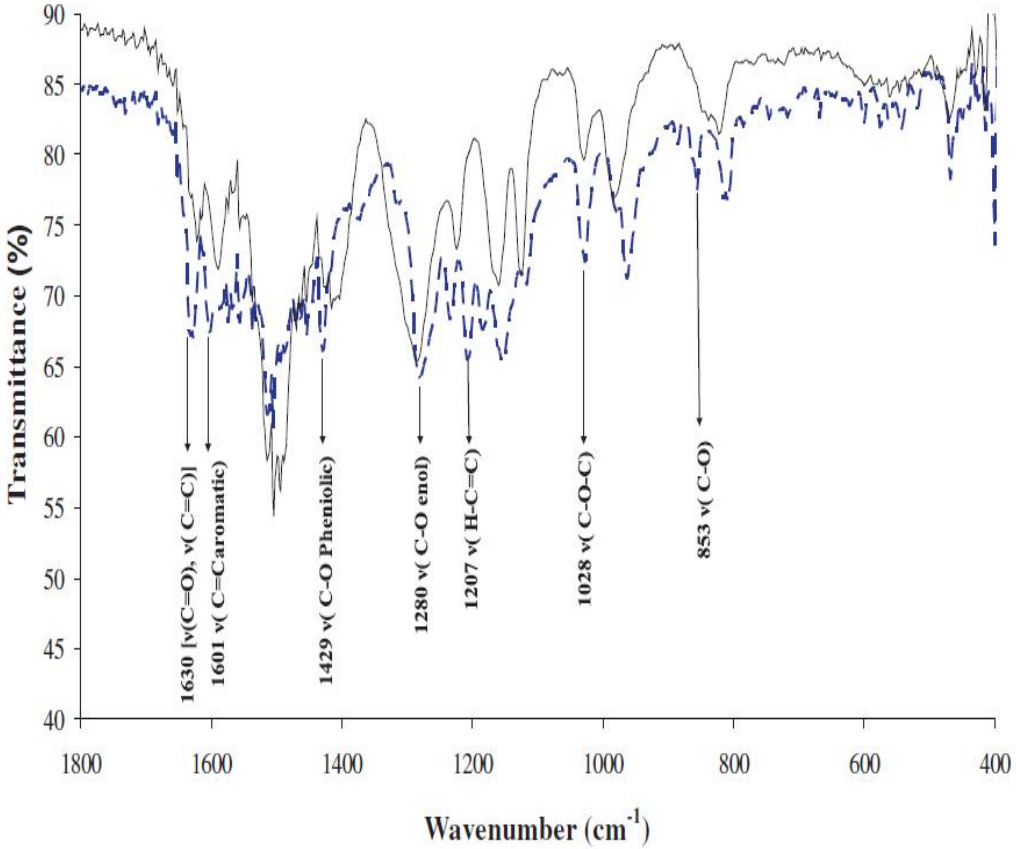
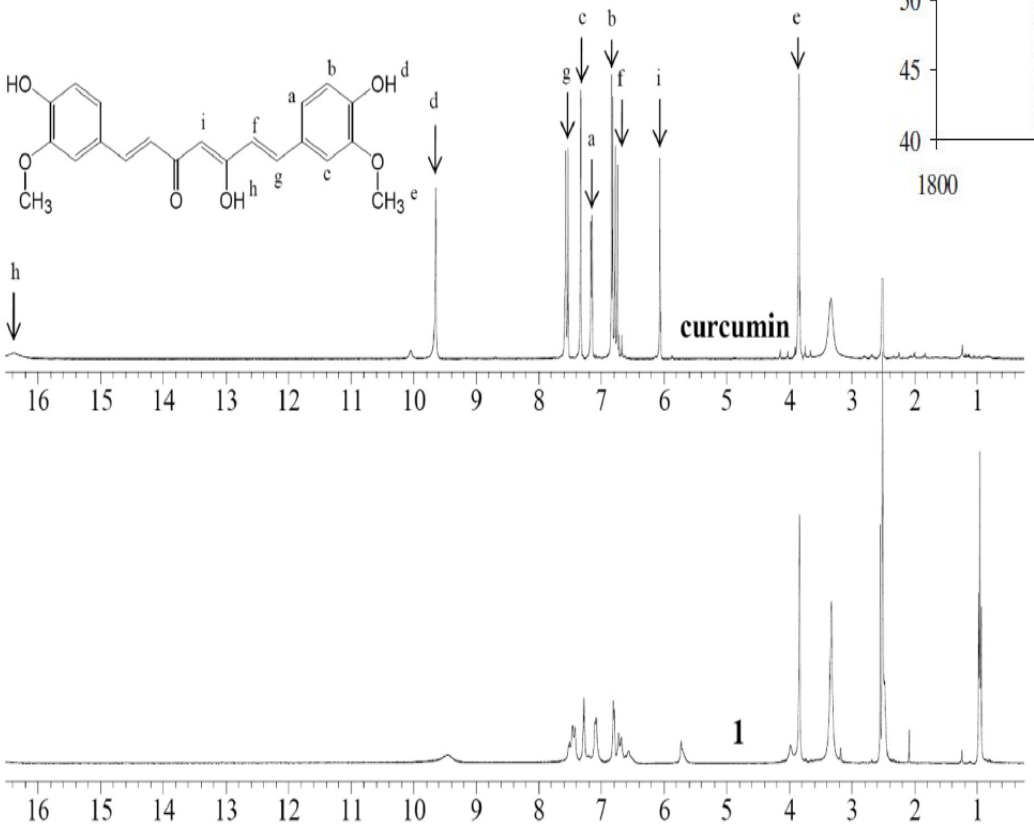
FT-IR



^{1}H-NMR



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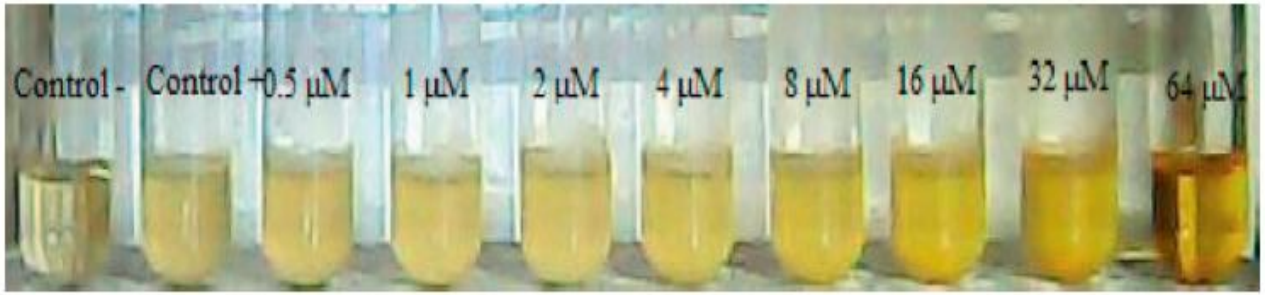
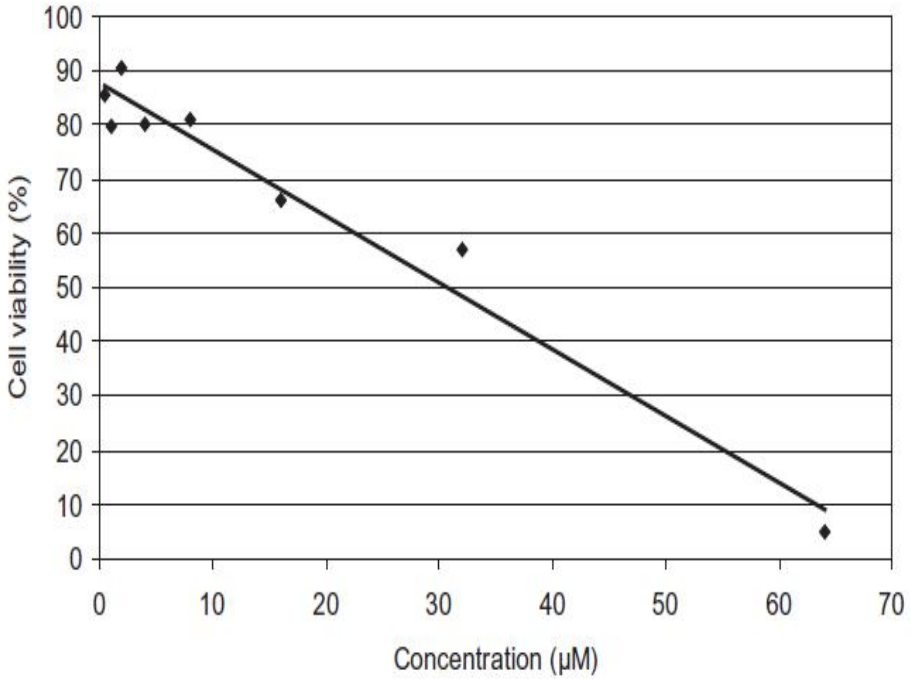
Antimicrobial activity *P. aeruginosa*





MIC $ZnI_2(Curc)_2$] 71.3 µM (75.3 µg/mL)
MIC curcumine: 339 µM (125 µg/mL)

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Effect on biofilm formation by packaging material

The material reduces the microbial load upon treatment with polystyrene@curcumin: 7.5%
polystyrene@[$ZnI_2(Curc)_2$] :14.7%

The material causes reduction in the viability of biofilm bacteria by polystyrene@curcumin: 2.4%
polystyrene@[$ZnI_2(Curc)_2$] :23.6%

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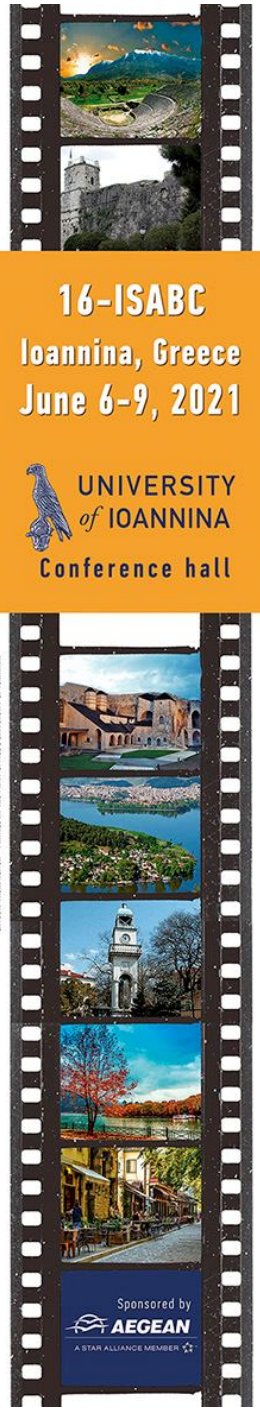

16th International Symposium on Applied Bioinorganic Chemistry

16-ISABC
Ioannina, Greece
June 6-9, 2021

UNIVERSITY of IOANNINA

Conference hall

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2. Metallomics, Metalloproteins Structures
3. Metals Complexes Interaction with RNA, DNA or Proteins
4. Bioinorganic Biomaterials
5. Biomimetic and Bioinspired Bioinorganic Chemistry and Energy Conversion
6. Metal Toxicology and Metals in Environment
7. Biophysical, Biochemical and Spectroscopic Methods in Bioinorganic Chemistry

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